

Structure of a Triple Helical DNA with a Triplex-Duplex Junction

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Extended purine sequences on a DNA strand can lead to the formation of triplex DNA in which the third strand runs parallel to the purine strand. Triplex DNA structures have been proposed to play a role in gene expression and recombination and also have potential application as antisense inhibitors of gene expression. Triplex structures have been studied in solution by NMR, but have hitherto resisted attempts at crystallization. Here, we report a novel design of DNA sequences, which allows the first crystallographic study of DNA segment containing triplexes and its junction with a duplex. In the 1.8 Å resolution structure, the sugar-phosphate backbone of the third strand is parallel to the purine-rich strand. The bases of the third strand associate with the Watson and Crick duplex via Hoogsteen-type interactions, resulting in three consecutive C(+).GC, BU.ABU (BU = 5-bromouracil), and C(+).GC triplets. The overall conformation of the DNA triplex has some similarity to the B-form, but is distinct from both A- and B-forms. There are large changes in the phosphate backbone torsion angles (particularly gamma) of the purine strand, probably due to the electrostatic interactions between the phosphate groups and the protonated cytosine. These changes narrow the minor groove width of the purine-Hoogsteen strands and may represent sequence-specific structural variations of the DNA triplex.